

Tolerance to *Theileria parva* infection



from Liam Morrison

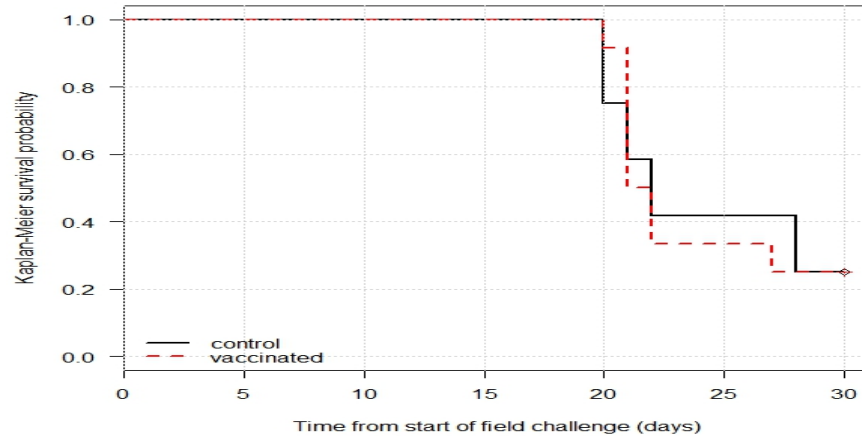
Importance of ECF

- Occurs in 12 countries in eastern, central and southern Africa
- Losses of \$300M; 28M of 47M cattle at risk
- Loss through mortality, morbidity
- Barrier to improved genetics
- Current control – Acaricides; ITM vaccine
- Improved control - ??

ITM Vaccine experiment - CIDLID

Outcome –

	Vaccinated	Control
Died/tx.	9	9
Survived	3	3



Vaccine experiment

ILRI Nos	SIRE	DAM	Deaths		Survivors
			20-22 dd	27-28 dd	
BJ025	SA3167	Bow474			25
BJ028	SA3167	61705K			28
BJ029	SA3167	43305H			29
BJ036	SA3167	Bow672			36
BJ024	BIY762	Bow645	24		
BJ026	BIY762	Bow685	26		
BJ027	BIY762	Bow348		27	
BJ033	BIY762	Bow311	33		
BJ042	BIY762	Bow624			42
BJ048	BIY762	Bow333	48		
BJ031	SA770	18807D	31		
BJ038	SA770	16906c	38		
BJ045	B764	Bow368	45		
BJ047	B764	Bow906	47		
BJ039	B764	Bow384	39		
BJ034	B1409	44304H	34		
BJ035	B1409	35304F		35	
BJ041	B770	Bow343	41		
BJ046	B770	Bow421	46		
BJ043	B291061E	Bow158			43
BJ044	B291061E	10507C		44	
BJ049	B291061E	Bow494	49		
BJ037	B09607C	40905H	37		
BJ030	BIY469	Bow104	30		
control					
vaccinated					

Summary of F1 field trials

		Survived	Died / Tx	% Survived	Fisher's Exact p
Trial 1	Progeny of ZI3167	3	0	100	
	Control	0	9	0	<0.01
Trial 2	Progeny of ZI3167	4	6	40	
	Control	1	13	7.7	0.12
Trial 3	Progeny of ZI3167	12	3	80	
	Control	0	11	0	<0.001
Combined	Progeny of 3167	19	9	68	Combined p (Stouffer's method)
	Control	1	33	4	<0.001

Field trial site in Ol Pejeta



Time to pyrexia

	Progeny	Control	p
Phase 3	18	15.7	0.098-0.132
Phase 4	15.7	14.3	0.000-0.001
Phase 5	14.6	12.8	0.006-0.015

Peak pyrexia

	Progeny	Control	p
Phase 3	40.6	41.3	0.122-0.151
Phase 4	41	41.7	0.024-0.040
Phase 5	40.7	41.2	0.025-0.035

Pyrexia intensity

	Progeny	Control	p
Phase 3	0.67	1.14	0.02-0.04
Phase 4	1.18	1.62	0.042-0.079
Phase 5	0.72	0.99	0.018-0.039

F2 sires



F2 trial – progeny of three sons of ZI3167

	Survived	Died/ Tx	% Survived	Fisher's Exact p
F2 Progeny	17	7	71	
Control	1	6	14	0.012

Not entirely novel:

'... the partial Theileria tolerance of the Ankole is, to a great extent, genetic.' (Paling et al., 1991)

'... Zebus born to dams from an ECF-endemic area showed a better ability to to control the course of the disease than cattle from ECF free areas.' (Ndungu et al., 2005)

... plus several others

Very important findings

- Alleles will assist in selecting tolerant animals
- Mechanism → new approaches to control

Focus is on identifying causative alleles

Genomic analyses

Resources

- Mixture of WGS and HD SNP array data for 117 animals
- 28 F1 progeny of 3167 plus phenotypes
- 51 F2 (of confirmed F1 sires 853, 919, 1481) plus 24 phenotypes
- 7 possible 3rd degree relatives, 4 sired by 786
- 34 control genotypes plus phenotypes
- Inferred paternal origin of haplotype blocks.

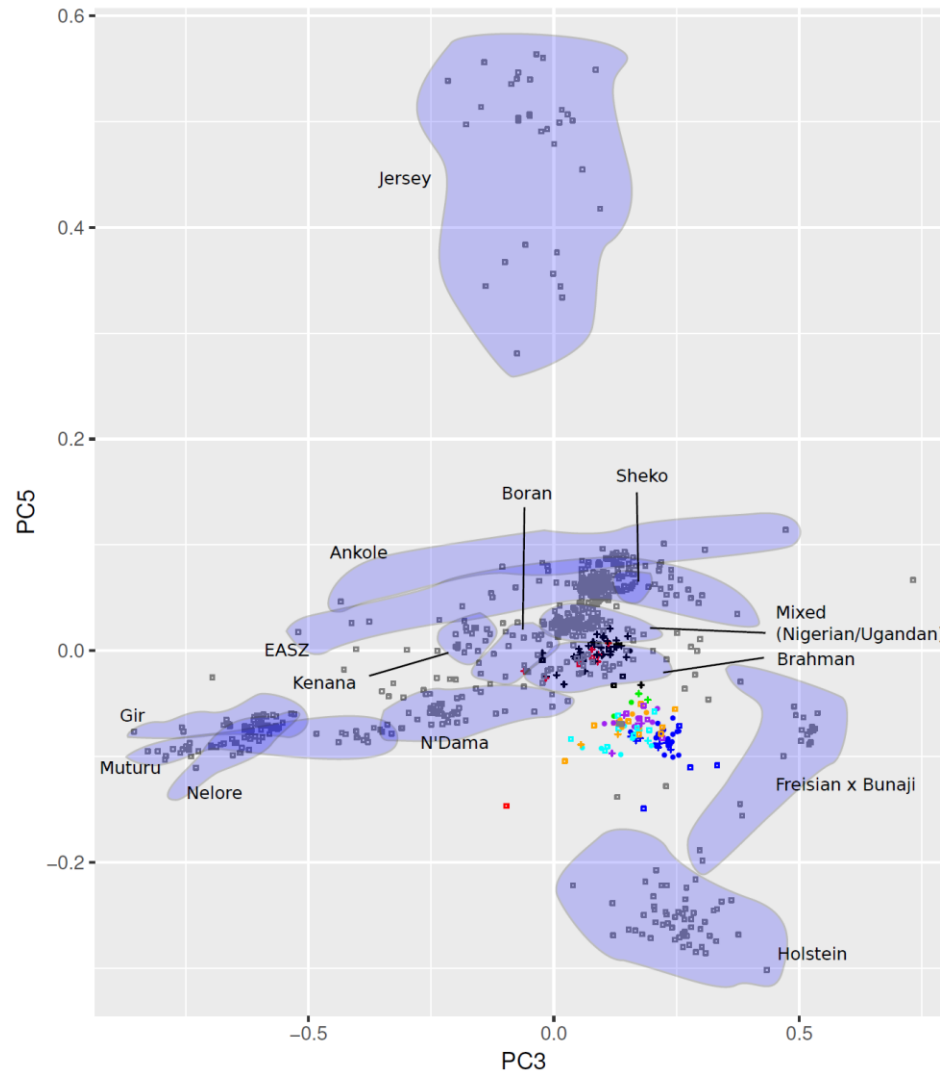
Genomic analyses

Linkage analysis

-No consistent signal associated with survival status across F1 and F2 groups

-However, various statistical tests of different phenotypic variables returned different genomic regions :

- Strongest - chr. 4 region linked to pyrexia onset
- Apoptosis
- Cell proliferation
- Interleukin production
- Cytokine signalling pathways



• Adamawa Gudali Nigeria	• 786 halfsib (3167 Cousin)
• Red bororo Nigeria	• 919 halfsib
• Nganda Uganda	• 853 halfsib
• Ankole Uganda	• 1481 halfsib
• NDama Nigeria	• Brahman
• Bunaji Nigeria	• Gir
• Serere Zebu Uganda	• Holstein
• Karamojong Zebu Uganda	• Jersey
• Azawak Nigeria	• NDama Guinea
• Freisan-Bunaji Nigeria	• Nelore
• Keteku Nigeria	• Muturu Nigeria
• Sokoto Gudali Nigeria	• Ankole
• Wadara Nigeria	• OH Boran
• Kuri Nigeria	• Kenana
• Sahiwal Zebu Uganda	• Muturu
• 3167 halfsib	• NDama
• EASZ	• Ogaden
• Control	• Sheko
• 3167 Unknown	

• Lived
+ Died
■ Unknown

Planned activities

1. Phase 7 field study
2. Genomic population study
3. Phenotypic indicators
4. Nucleus herd
5. Cattle-derived challenge



ILRI

Phil Toye

Annie Cook

Tatjana Sitt

Gideon Ndambuki

Maureen Chepkwony

Jane Poole

RI

James Prendergast

David Wragg

Ivan Morrison

OL PEJETA

Giles Prettejohn

Richard van Aardt

Joseph Mathenge

Mila Meshani

Robert Parkilei Parmashu

KAPITI

Simon Kibiru

Cosmas Marete

DFID _ BBSRC / ILRI L&F CRP – AH & LG / BMGF